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Purpose/Objective: Hippocampal-avoiding whole brain radiotherapy (HA-WBRT) for multiple brain metastases may prevent treatment-related cognitive decline, compared to standard WBRT. Reduction in hippocampal volume over time has been shown to be significantly related to decline in memory and learning. This study aims at exploring brain volume changes after whole brain radiotherapy with hippocampal avoidance (HA-WBRT).
Materials and Methods: 22 patients who had been assigned to HA-WBRT following clinical indication received MRI before and up to 19 months after treatment (Mean = 5 months). Observer-independent, automated volumetry of the hippocampi, the lateral ventricles, and the whole brain was performed on 77 MRI data sets using Matlab and statistical parametric mapping (SPM8). Longitudinal volumes have been tested for significant brain changes after HA-WBRT. Linear mixed models were computed with regional volumes as dependent variables and predictor variable time with random intercepts and slopes for time across subjects and variance components as covariance structure (controlling for age). Volume change rates after RT have been calculated for each region.
Results: At the group level, hippocampal [-0.02 ml (-0.19%) per month] and whole brain volumes [-2.03 ml (-0.19%) per month] showed decreases which did not reach significance. By contrast, the lateral ventricles significantly expanded [p < 0.0001; +1.2 ml (3.6%) per month (43% per year)].
Conclusions: In this pilot study we observed no significant hippocampal atrophy after HA-WBRT. The lateral ventricles, however, expanded after treatment, indicating cerebral atrophy at a higher rate than reported in the literature on healthy subjects. While brain tissue degeneration seems to occur in this group of patients, hippocampal tissue is spared from this process.

PO-0802

Outcomes of fSRT compared to SRS for brain metastases by using volumetric surrogates for fractionation

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Purpose/Objective: Local control (LC) rate is inversely related to the volume and size of the brain metastases treated with SRS. We aimed to demonstrate the potential role of fSRT with increasing volumes in order to improve LC.
Materials and Methods: Between 2001-2004, 180 patients with brain metastases were treated with stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (fSRT). Sixty-five percent were treated for newly diagnosed, whereas 35% for progressive brain metastases after previous whole brain radiotherapy. Median number of metastases was 2 and distributed as single 43%, 2-3 mets 33%, 4-10 mets 16% and >10 mets 8%. Median age was 59 years (29-87 years); 38% was female, 62% male. Primary tumor site was lung in 65%, breast in 16%, gastrointestinal 7%, kidney 5%, melanoma 2% and others 5%. Patients were grouped according to the diameter of the largest metastasis as ≤10mm in 15%, 11-20mm in 36%, 21-30 mm in 31% and >30 mm in 18%. Patient fixation was made with thermoplastic masks. CT and MR simulation with contrast was made on-site at the same day. GTV was equal to PTV. All treatments were performed on TrueBeam STx with Novalis (Varian, Palo Alto, USA and BrainLAB AG, Feldkirchen, Germany) using flattening filter free beams and non-coplanar multiple partial arcs. Decision for fractionation was made according to the size of the largest metastasis, cumulative volume and location of the metastases. Percentage of fSRT in diameters of ≤10mm, 11-20mm, 21-30 mm and >30 mm were 15%, 57%, 91% and 100%. Median peripheral doses were 18 Gy for single fraction (14-20 Gy), 24 Gy for 3 fractions (18-27 Gy) and 30 Gy for 5 fractions (22.5-40 Gy) treatments.
Results: At a median follow-up of 6 months (1-38 months) median overall survival (OS) was 12 months for the whole group (newly diagnosed group 13 months, progressive group 8 months, p=0.004). OS curves separated significantly in patients with ≤20mm, 21-30 mm and >30mm diameters with median OS as 17, 12 and 7 months, respectively (p<0.01). LC at 1 year for the newly diagnosed patients was 79%, and for the progressive patients 69% (p<0.01). One-year LC rate for ≤10mm, 11-20mm, 21-30 mm and >30 mm diameter was 100%, 74%, 70% and 69%, respectively (p=0.02, for ≤10mm vs others). Specifically in the group with large metastases (>30 mm, n=33) all of whom were treated with fSRT, one-year LC rate was 100% for the newly diagnosed patients, and 47% for progressive patients. Salvage treatment was performed as SRS in 25 patients (14%), WBRT in 7 patients (4%) and surgery in 2 patients. Repeat SRS to the same target was done in one patient. Radionecrosis was observed in 10 patients (5.6%), and all were treated with steroids or bevacizumab without surgery.
Conclusions: Single fraction SRS can achieve high local control for small brain metastases. For larger metastases fSRT can successfully replace SRS with improved LC and lower toxicity.

PO-0803

Optimization of GTV definition and treatment planning in lung-sparing VMAT for pleural mesothelioma

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Purpose/Objective: Our purpose is to optimize RT target definition and treatment planning in lung-sparing VMAT for malignant pleural mesothelioma. In this multistep process, we identified 2 main objectives: 1) to investigate which imaging modality is optimal for GTV definition (CT, PET/CT or MRI); 2) to develop a model able to identify the maximum safe dose escalation level for each patient.
Materials and Methods: Sixteen consecutive stage I-IV MPM patients were retrospectively identified from an institutional database and included. For the contouring phase, a CT with IV contrast, ^{18}FDG-PET/CT and MRI were obtained. CT was rigidly co-registered with PET/CT and with MRI. Three sets of pleural GTVs were defined: GTV_{CT}, $GTV_{CT+PET/CT}$ and GTV_{CT+MRI}. 'Quantitative' and 'qualitative' evaluations of the contoured GTVs were performed. For the planning phase, the GTV with the lower 'geographical miss' rate was chosen to generate the PTV. The first 6 consecutive left-sided and right-sided patients were selected, for a total of 12 patients. For all patients, VMAT plans were created. Prescription dose was 50 Gy in 2-Gy fractions delivered to the PTV, and progressive dose-escalation steps (with 4 Gy increment) were attempted. The correlation between the contralateral/ipsilateral lung volume ratio and the PTV/total lung volume ratio with the achieved PTV dose was investigated.
Results: Compared to CT, PET/CT identified geographical miss in 10/16 patients, and MRI avoided frank GTV underestimation in 15/16 patients. In 15/16 patients, MRI modified also PET/CT contours. Differences in mean volumes ranged from 1.7 to 5% and were not significantly different. Mean Jaccard index (indicating lower concordance) was lower in MRI-based contours versus all the others. For 10/12 patients was possible to generate a 50 Gy VMAT plan. The maximum achievable dose was 54 Gy, 58 Gy and 62 Gy in 7, 4 and 1 patients, respectively. A significant correlation between the contralateral/ipsilateral lung volume ratio and the PTV/total lung volume ratio with the achieved PTV dose was found (p=0.05).

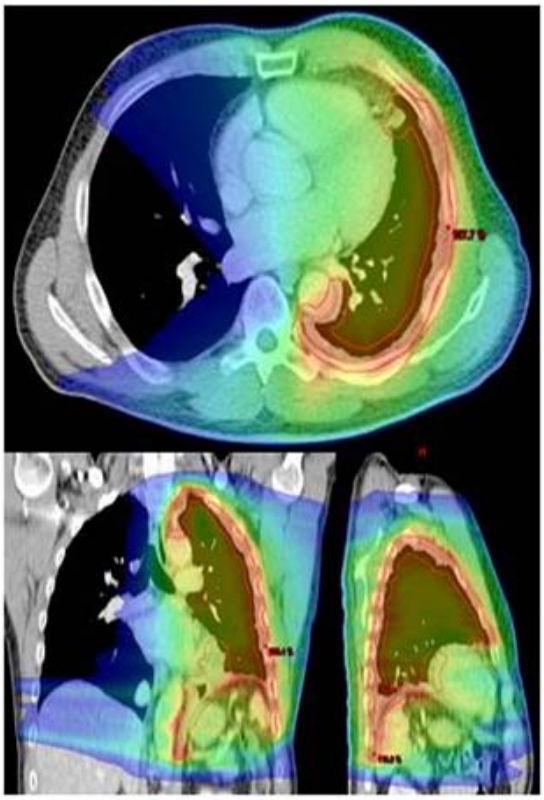

Figure 1. Axial, coronal and sagittal view of a 54 Gy VMAT plan.

Conclusions: To the best of our knowledge, this is the first study showing that the integration of MRI into the target volume definition in MPM may allow improving the accuracy of GTV delineation and reducing the probability of geographical misses. Patients with a higher ratio of contralateral/ipsilateral lung volume and lower ratio of PTV/total lung volume are less likely to achieve a therapeutic RT dose.

PO-0804
Volumetric Total Lymphoid Irradiation: step-up an effective treatment for stem cell transplantation in lymphoma

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Purpose/Objective: For patients with relapsed/refractory Hodgkin's disease (HD) and non-Hodgkin lymphoma (NHL), autologous hematopoietic stem cell transplantation (aHSCT) is the standard of care. HD treatment by accelerated hyperfractionated total lymphoid irradiation (TLI) with three-dimensional conformal radiotherapy (3D-CRT) has been investigated in dated clinical trials with good clinical outcomes. Today IGRT and IMRT allow the reduction of unbearable radiation dose to healthy tissues. Herein we report our preliminary clinical experience in planning and delivery of newly designed short-course hypofractionated TLI by Helical Tomotherapy (HT) followed by HDT and aHSCT.
Materials and Methods: From February 2011 to March 2012,